



Immune Responses and Pathogenesis of Crimean–Congo Hemorrhagic Fever: An Overview

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Dear Editor,

Crimean–Congo hemorrhagic fever (CCHF) is an emerging tick-borne (Ixodid ticks) viral infectious disease. CCHF is caused by RNA virus that is a member of genus *Nairovirus* in the family *Bunyaviridae* as the greatest virus family. This infection has vast geographical distribution in Asia, Africa and some parts of Europe. This agent can be transmitted to humans in several ways such as direct contact with infected body fluids and blood or ticks. Small mammals are the main hosts of the virus. Although, domestic livestock present no clinical sign, they can transfer the disease during the period of viremia. The acute form of the infection usually lasts for two weeks and is characterized by prolonged weakness and confusion. Generally, the most common clinical signs and symptoms of this severe hemorrhagic viral disease include fever, headache, back pain, sore eyes, petechial rash, vomiting, and diarrhea. The mortality rate varies from 5% to 50% (1). Death is generally due to hemorrhagic and neurological complications (Figure 1). The pathogenesis of CCHF appears to be multifactorial, and it is poorly understood. However, an interaction between the virus and the host cells is known to be responsible for the pathogenesis of infection. The hepatocytes and endothelium are supposed to be the main target cells in CCHF. The infection of the hepatocytes leads to reduced synthesis of albumin as the main protein of human blood plasma, which can cause edema. Moreover, this hepatocyte dysfunction accounts for abnormal liver function tests (LFTs) (2). Endothelial damage can deregulate stimulation of platelet aggregation; on the other hand, it may contribute to coagulopathy. In addition, disseminated intravascular coagulation (DIC) is administrated by the activation of the clotting cascade that results in the formation of blood clots in the vessels. This pathological phenomenon can contribute to the activation of coagulation during CCHF (3). This virus can also infect antigen-presenting cells (APCs). The infected macrophages or dendritic cells (DCs) release soluble factors such as cytokines. Several studies in CCHF reported that the release of tumor necrosis factor alpha

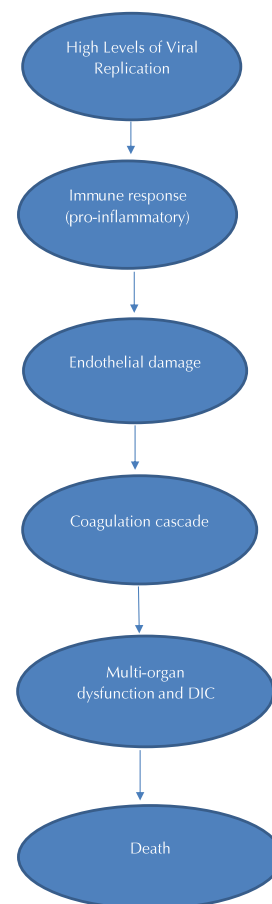


Figure 1. Pathogenesis of Crimean-Congo Hemorrhagic Fever.

(TNF- α), Interleukin 6 (IL-6) and IL-10 may be engaged in the pathogenesis and outcome of the disease (4). TNF- α affects the endothelium and stimulates anti-fibrinolytic action. TNF- α and IL-6 are associated with DIC. IL-10 which can suppress the immune response to infection also allows high replication of the virus. Watson et al showed that the IL-12/IL-10 ratio is perhaps a useful procedure to approach the state of the immune system in CCHF (5,6). Some studies showed that there is a positive correlation between viral load and few proinflammatory cytokines and



also elevated levels of IFN- γ in cases with fatal outcomes of CCHF (7). Therefore, there are many vague points in the pathogenesis of CCHF that require further studies. In addition, a complete understanding of the pathogenesis may lead to more effective diagnostic and treatment designs.

Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

Not applicable.

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